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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,631	02/10/2004	Kevin S. Currie	09580.0008-00000	1748

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EXAMINER	
TUCKER, ZACHARY C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,631	CURRIE ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *36-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10Feb06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

A Requirement for Restriction of the instant application was mailed 27 January 2006. Applicant's election with traverse of the invention of Group I, in the reply filed on 10 February 2006, is acknowledged. The traversal is on the grounds that no method according to the instant claims can be practiced with a materially different product than the products set forth in Group I of the Requirement. This is not found persuasive because if it were true, then no Requirement for Restriction between a product and a process of using that product would ever be proper. If a process of achieving the effect specified in the process of using the product is practicable with some product materially different than the product according to the present invention, then condition "(1)" as was set forth on page 2 of the Requirement for Restriction letter has been met.

Applicants' counsel further argues that all prior art relevant to determining the patentability of all of the instant claims would be considered in determining the patentability of the compounds according to Group I. This is not entirely true, because methods, which constitute restriction Groups II and III, require a search to determine the state of the art with respect to the methods specified therein, to determine compliance with the first paragraph of 35 U.S.C. 112. Subject matter as set forth in Group I does not require this additional aspect of the search, so the search required for each one of the restriction Groups is not the same.

Applicants' counsel, lastly, argues that no serious search burden exists. According to the MPEP §803, "...a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation of separate classification, or

separate status in the art, or a different field of search as defined in MPEP § 808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by the applicant." No rebuttal of the examiner's showing of separate classification and separate status in the art has been attempted. Thus, a serious burden has been established.

A Requirement for Restriction between methods and compounds is sound and finds its basis clearly set forth in the MPEP. The requirement is still deemed proper and is therefore made FINAL. Accordingly, claims 36-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Upon finding that the elected Group is in condition for allowance, applicant will be entitled to rejoinder of Groups II and III. At such time, the Requirement for Restriction between Groups I, II and III will be WITHDRAWN.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-35 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Every claim 1-35 includes the phrase "or form thereof" in reference to the compound of Formula I. Exactly what type of form this phrase is referring to is unclear, as only examples of what applicants intend the term includes are provided at page 14, in paragraph [0060]. In its broadest reasonable interpretation, "pharmaceutically acceptable forms thereof" embraces chemical derivatives of the compounds of Formula

(I) of indeterminate structure. Should the term be exchanged for the language of paragraph [0060] of the instant specification, rejection of claims 1-35 and 60 under the first paragraph of this statute will be necessary, because prodrugs, solvates, crystal forms, polymorphs, chelates, clathrates and mixtures thereof are *not* enabled by the disclosure.

Specification

In the Requirement for Restriction letter, objection to the title, on grounds it is not descriptive of the invention, was set forth. At applicants' request, this objection will be held in abeyance until such time as the claims are indicated as being in allowable form.

Comments inquiring whether the variable Z_1 was intended to be part of the instant claims were also included in the Requirement for Restriction letter. Applicants' counsel has indicated in reply that although Z_1 is part of the structure of compounds according to the present invention, that variable in the compounds according to the instant claims is a covalent bond, hence it is not shown in the structure diagram of the claims.

Information Disclosure Statement

An Information Disclosure Statement was filed by applicants on 10th February 2006. References cited in the statement have been considered by the examiner, and signed and initialed forms PTO-1449 to that effect are enclosed with this Office action. It is noted that fourteen documents which are search reports and written opinions of foreign patent offices, for claims in different international applications, presumably applications corresponding somehow to the instantly claimed subject matter. These citations are first of all irrelevant to the examination of the presently claimed subject

matter because the United States Patent Office is not beholden to decisions or opinions rendered by any foreign or so-called "international" authority, secondly, because the *claims* which are the subject of these reports and opinions are not included therewith (save one of the documents, which does include a copy of claims) and third, *how* it is that the international applications which are being referred to in the reports and opinions are related to the instant application is not explained. All of these international search reports and opinions have been lined through, because they are not publications, and as such are improperly cited because no publication date is listed (required by 37 C.F.R 1.98(b)(5)). The examiner has conducted a cursory review of the material, however, and it has been placed in the file wrapper.

Allowable Subject Matter
~and~
Comments on Withdrawn Claims

Claims 1-35 and 60 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. Deletion of the word "form" in all occurrences (and from the corresponding withdrawn claims), and replacing it with the word "salts" ("pharmaceutically acceptable salts thereof") would overcome the rejections at hand. Introduction of language along the lines of "solvates thereof" or "prodrug (forms) thereof" would prompt rejection of the claims under the first paragraph of 35 U.S.C. 112, for non-enablement of those solvates and prodrugs.

No prior art disclosure anticipating or rendering obvious any compound according to claims 1-35 and 60 was found. Closely related copending application serial number 10/776,002 (also being examined by this examiner) is does not present any double

patenting issues, because of the definition in variable R_1 being different and non-overlapping in the respective applications. R_1 is an acyclic substituent or phenyl or a benzo-fused nonaromatic heterocycle in the instant claims, while R_1 is limited to pyrimidinyl or pyridyl in the claims of the aforementioned copending application.

As indicative of the closest prior art, the examiner would bring to applicants' attention US 6,518,270 (Amin et al – disclosing gastric acid secretion-inhibiting compounds) and US 6,919,341 (Paruch et al – kinase inhibitors). Other relevant prior art, disclosing various imidazopyrazines or closely related bicyclic heteroaryl core structures are disclosed in the aforementioned Amin et al and Paruch et al patents and references, which are cited in the Information Disclosure Statements filed in the instant case (filed 10 February 2006, 10 May 2004 and 5 November 2004).

The basis for the novelty of the instant claimed compounds is the $-Z_2-R_2$ group bonded to the "X" – containing ring at the 6-position of the imidazo[1,2-a]pyrazine ring system. Although Z_2 can collapse down to a single bond, the presence of R_2 requires at least an unsubstituted phenyl ring that is neither disclosed nor suggested in the prior art. Most prior art disclosures of similar kinase inhibitors are based on a structure wherein an oxygen or nitrogen atom linker is present at the 8-position of the imidazo[1,2-a]pyrazine ring system, as opposed to the compounds according to instant claims, wherein an aromatic ring is directly bonded to the 8-position (and the compounds claimed in copending application serial number 10/776,002).

It is noted that the instant application includes (now withdrawn) claims drawn to the treatment of "cancer," generally, which includes *all* cancers, treatment of "autoimmune disease," generally, which includes *all* autoimmune diseases, and

"neurodegenerative disease," generally, which includes *all* neurodegenerative diseases. Only *in vitro* demonstrations of pharmacological activity of the compounds according to the present invention are provided in the instant specification (paragraphs [00163] – [00180]). The most clinically relevant example of biological activity is the assay of inhibition of the growth of tumor cells, specifically MCF-7 cells, which are human breast cancer cells, and HCT-15 which are colorectal adenocarcinoma cells. These test results are predictive for activity against only the type of cancer tissue assayed, namely breast cancer and colorectal cancer, not *all* cancers. Evidence will presented to that effect if need be.

As for the treatment of the full scope of all autoimmune diseases and all neurodegenerative diseases, it is unbelievable on its face that a single agent could provide a means for treating all such diseases.

Claims drawn to "modulation the activity of Hsp90 complex" are subject to rejection both under the first and second paragraphs of 35 U.S.C. 112, because the step of "contacting cells" with compounds according to the present invention reads on doing so in a live animal as well as *in vitro*, and as such the claim is a method of treating some unspecified disease.

It is recommended that claims drawn to treatment of diseases be cancelled. Claims drawn to pharmaceutical compositions comprising a claim 1 compound and a pharmaceutically acceptable carrier, and claims drawn to an *in vitro* method of modulating Hsp90 activity, or modulating the binding of ATP with Hsp90, *in vitro*, would be allowable. An *in vitro* method must state in the *preamble* that the claim is drawn to an *in vitro* method, as opposed to the construction of instant claim 45,

wherein the phrase "*in vitro*" appears at the end, which does not limit the method only to *in vitro* methods.

A pharmaceutical composition comprising "instructions for using the composition to treat a patient suffering from an [*sic*] disease or disorder responsive to Hsp90 complex modulation," such as instant claim 38 and claims depending therefrom, would be the subject of rejections under both the first and second paragraphs of 35 U.S.C. 112.

Claim 37 specifies a pharmaceutical composition, wherein the composition is selected *inter alia* from "a tablet" and "a pill." Tablets and pills are the same type of dosage from. One or the other should be chosen. Tablet is the more technical term.

Applicants should not interpret any of the preceding comments as an indication that the withdrawn claims have been examined, only that they have been *read*, to determine what they cover. The MPEP directs the examiner to do so, when making requirements for restriction, in chapter 814.

Conclusion

It is the policy of the Office to notify applicants' counsel by phone in cases where the only rejections being set forth in a first action on the merits are indefiniteness rejections (112, second paragraph), so that amendment to place the case in condition for allowance on the first action might be authorized. The examiner did make an attempt to contact Lauren L. Stevens, applicants' counsel, but no telephone number is listed on correspondences signed by her, and the telephone number on file in "PALM," which is (650) 849-6500 is disconnected.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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